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The renal osteodystrophy pattern in Brazil and Uruguay: An overview

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The renal osteodystrophy pattern in Brazil and Uruguay: An overview.

Background. The prevalence of the types of renal osteodystrophy (ROD) has changed in the last two decades. This study evaluates the prevalence and determining factors of the types of ROD in two countries in South America.

Methods. Symptomatic patients who underwent bone biopsies for diagnostic purposes (1985 through 2001) were included in the study. In Brazil, a total of 2340 patients were reviewed, 93.1% on hemodialysis (HD), and 6.9% on continuous ambulatory peritoneal dialysis (CAPD). In Uruguay, 167 patients on hemodialysis were included. Uncalcified bone samples were analyzed in order to diagnose the different types of ROD.

Results. Comparing the 1980s to the 1990s, the prevalence of Brazilian patients with hyperparathyroid bone disease (HP) increased from 32.3% to 44.0%, while Al overload decreased from 61.3% to 42.4%. A logistic regression analysis showed that the main factors associated with HP included female gender, age of less than 40 years, black patients, longer time on dialysis, and absence of Al overload. In Uruguay, HP also increased over time from 31.8% to 70.5% ($P < 0.05$), while Al overload decreased from 42% to 27% ($P < 0.05$).

Conclusion. A better control of Al overload may lead to a change in histologic pattern, as evidenced by the increasing prevalence of HP.

Renal osteodystrophy (ROD) in patients with chronic renal failure on dialysis is a major long-term complication with high morbidity. Clinical and histologic forms of ROD comprise a wide spectrum that includes predominant high turnover states, such as hyperparathyroid bone disease (HP), mixed bone disease (MBD), low turnover osteomalacia (OM), and adynamic bone disease (ABD). The mechanisms underlying the development of these skeletal disorders are multifactorial and controversial, whereas the effects of aluminum (Al) overload have been well established [1]. The prevalence of different types of ROD in the diverse geographical areas [2] has changed during the past two decades. Several conditions, including demographic and geographical factors, different preventive measures, and therapeutic management of the dialyzed patients, in addition to no uniformity of the tools and diagnostic criteria, may contribute to the outline of the ROD profile [3–7]. Although bone histomorphometry is the most reliable diagnostic method, in recent years, noninvasive methods of ROD diagnosis like iPTH and other biochemical markers to assess bone metabolism have elicited more rational criteria for the need of bone biopsy [8].

The aims of this study were to analyze the prevalence of the different forms of ROD over time in symptomatic dialyzed patients who underwent bone biopsy in Brazil and Uruguay, and to identify risk factors that could be associated with the pattern of ROD.

METHODS

A total of 2507 bone biopsies obtained over 16 years in Brazil and Uruguay were studied. Bone analysis was performed in three units (two in São Paulo and one in Rio de Janeiro, Brazil). In Brazil, a total of 2340 bone biopsies from patients from various geographic areas (93.1% on HD and 6.9% on CAPD) were reviewed. The majority of patients were white (53.8%), followed by mullato (35.0%), and black (10.2%). There were 1120 female (47.9%) and 1220 male (52.1%), with a mean age of 41.2 ± 14.3 years, mean dialysis duration of 73.7 ± 57.1 months. In Uruguay, we reviewed 167 bone biopsies from white patients on HD. Ninety-three patients were female (55.7%) and 74 were male (44.3%), with a mean age of 54.0 ± 13.0 years, and mean dialysis duration of 53.0 ± 33.0 months.

Bone samples from the anterior iliac crest were obtained and processed as previously described [2]. Informed consent was obtained in all patients. For iron

Key words: secondary hyperparathyroidism, aluminum, dialysis, bone biopsy.

Table 1. Histologic diagnosis, number, and percentage according to country of origin and period of bone biopsy

Country	Period *years*	HP *N* %	MBD *N* %	OM *N* %	ABD *N* %
Brazil	P1 85–90	119 (32.3)[a,b]	61 (16.6)[b]	121 (32.9)[a,b]	67 (18.2)
	P2 91–96	365 (42.6)	183 (21.4)	174 (20.3)[c]	134 (15.7)[c]
	P3 97–01	491 (44.0)	267 (23.9)	130 (11.7)	228 (20.4)
Uruguay	P1 85–90	21 (31.8)[a,b]	11 (16.6)	24 (36.6)[a,b]	10 (15)
	P2 91–96	49 (58.3)	17 (20.2)	4 (4.5)	14 (17)
	P3 97–00	12 (70.5)	0 (0)	0 (0)	5 (29.5)

[a] vs. P2 $P < 0.01$
[b] vs. P3 $P < 0.05$
[c] vs. P3 $P < 0.01$

detection after 1998, São Paulo units changed from aurin tricarboxylic acid (Aluminon®) to solochrome azurine staining for detection of Al associated with Pearls staining. Al overload was considered positive when Al surface was greater than 30% of total trabecular surface.

Patients were classified as predominantly HP, MBD, OM, and ABD, according to histologic analysis.

We analyzed the prevalence of the types of ROD in three periods: 1985–1990 (P1), 1991–1996 (P2), and 1997–2001 (P3). In Brazilian patients, we also analyzed the risk factors for each pattern of ROD. In Uruguay, aluminum dialysis water was analyzed in P2 and P3 only.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS for Windows, Version 8.0 (SPSS, Inc., Chicago, IL, USA), and data have been expressed as mean ± SD unless stated otherwise. For multiple comparisons of periods, Pearson Chi-Square and Exact Fisher tests were used. The multivaried analysis was performed by logistic regression for test risk factors. Values of P lower than 0.05 were considered statistically significant.

RESULTS

Data from Brazil

The prevalence of HP increased from 32.3% in P1 to 44.0% in P3 ($P < 0.05$). This increase was also observed in MBD (16.6% to 23.9%, P1 vs. P3, respectively, $P < 0.05$). On the other extreme of the ROD spectrum, OM decreased significantly (32.9% to 11.7%, P1 vs. P3, $P < 0.05$; and 20.3% to 11.7%, P2 vs. P3, respectively, $P < 0.01$). The prevalence of ABD increased from 15.7% to 20.4%, P2 vs. P3, respectively, $P < 0.01$ (Table 1). Al overload was present in 61.3% of the patients in P1, decreasing to 38.7% in P2 ($P < 0.0001$), and remained stable in P3 (42.5%, $P < 0.05$ vs. P1). Logistic regression analysis showed that the occurrence of HP was correlated with female gender (OR = 1.27, $P < 0.05$), age less than 40 years (OR = 1.37, $P < 0.01$), black patients (OR = 1.64, $P < 0.05$), time on dialysis more than four years (OR = 2.03, $P < 0.0001$), and lack of Al overload (OR = 3.17, $P < 0.0001$). Moreover, factors such as male gender, white race, older age, short dialysis history, and CAPD were associated with ABD (χ^2, $P < 0.005$). Bone pain, arthralgia, and myalgia were the most frequent symptoms in all patients. Fractures, muscle weakness, and myalgia were associated with OM (χ^2, $P < 0.005$). The frequency of bone pain, arthralgia, and fracture were less commonly observed in ABD patients (χ^2, $P < 0.005$). However, we did not find any differences in the frequency of fractures between ABD, HP, and MBD.

Data from Uruguay

Similar to Brazil, HP increased over time from 31.8% in P1 to 70.5% in P3 ($P < 0.05$) (Table 1). MBD was 16.6% and 20.2% in P1 and P2, respectively, and absent in P3. OM decreased from 36.6% in P1 to 4.5% in P2 ($P < 0.01$), and was absent in P3. Although not significant, the ABD tended to increase over the periods (15.0%, 17.0%, and 29.5%, respectively). Al overload was detected in all ABD patients in P1, 86.0% in P2, but only 20.0% in P3 ($P < 0.05$). Considering all bone biopsies, the Al overload decreased from 42.0% in P1 to 20.0% in P2 ($P < 0.05$), remaining stable in P3 (27.0%; NS). Concomitantly, the content of aluminum in the water for dialysis showed 88.0% of samples in P2 with Al concentration lower than 10 μg/L, and in P3, 97.0% of samples below 2 μg/L, showing an improvement in water quality. Data from P1 were missing.

DISCUSSION

This study describes the distribution of ROD pattern in Brazil and Uruguay. One should be reminded that bone biopsies were performed in patients who were symptomatic, or presented some clinical, radiologic, or laboratory test abnormalities. Therefore, we cannot compare our results with those obtained from studies performed in nonselected dialysis populations [9, 10]. We observed a similar tendency in both ROD profiles (e.g., an increase in HP and a decrease in OM). The increasing prevalence of HP could be related to longer survival on dialysis, which is a key determinant of secondary hyperparathyroidism [11]. In fact, in this study, one of the determinants of HP in Brazilian patients was longer time on dialysis. These findings are in accordance with

others [9–11]. Looking at the relationship between HP and other determining factors like gender, age, race, and Al overload, we observed more preeminent bone disease in young women, as did Cundy et al [12]. A possible explanation for this fact could be that estrogen has a direct action on parathyroid hormone gene expression, increasing parathormone secretion [13]. In relation to race, black patients were prone to developing HP [14]. It has been noted that blacks have lower serum 25-hydroxyvitamin D because melanin absorbs ultraviolet light and prevents formation of pre-vitamin D3 in the skin [15]. Moreover, Ghazali et al [16] recently demonstrated that low plasma 25-hydroxyvitamin D is a major risk factor for hyperparathyroidism. Another point was that the absence of Al overload was a determining factor of HP in our series. Al intoxication is known to exert marked changes in parathyroid function. Moreover, follow-up studies have demonstrated that the removal of Al is followed by increments in parathormone level [17, 18]. As presented in our study, the decrease of Al overload over time may contribute to the observed results.

With regard to ABD and some demographic factors, our data are in accordance to those of the literature. Thus, male gender, white race, older age, short dialysis history, and CAPD have been associated with ABD [19].

Finally, the prevalence of bone biopsies with Al overload has diminished significantly over time in both countries. During the last decade, reduction in the use of aluminum-containing phosphate binders and the improvement of dialysis water quality could be responsible for these results. As a matter of fact, the introduction of water treatment in all dialysis units in Uruguay after 1990 led to a better control of aluminum concentration in water for dialysis, contributing to the decreased prevalence of Al overload and OM. In Brazilian data, we could not observe a further decrease in Al overload in the last period studied (1997–2001). This could be due to the change of the Al staining techniques used by the two units in São Paulo, which have been responsible for the analysis of more than 80% of bone biopsies in Brazil. As we know, solochrome azurine is more sensitive than Aluminon® in detecting Al bone surface [4].

CONCLUSION

Our data revealed a reduction in the incidence of Al overload over time, which may contribute to the increased prevalence of HP observed. This change in the profile of ROD has already been observed in the recent past in developed countries. We may conclude that, despite the efforts in controlling Al overload, continuous preventive therapeutic strategies are necessary to avoid the disclosure of different and more severe types of ROD.

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